

FIG. 1-1

| | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|--|---|
| | | | | | | | | | | | | | | | | | | | |
| | * | | * | | * | | * | | * | | * | | * | | * | | * | | * |
| TG | ACT | TTG | TAT | ACT | TAA | CAA | CAT | CCT | GTA | GCC | GGG | TCT | CAG | GAC | ATC | AAG | | | |
| AC | TGA | AAC | ATA | TGA | ATT | GTT | GTA | GGA | CAT | CGG | CCC | AGA | GTC | CTG | TAG | TTC | | | |
| | T | L | Y | T | * | Q | H | P | V | A | G | S | Q | D | I | K> | | | |
| | | | 60 | | | | 70 | | | | 80 | | | | | 90 | | | |
| | * | | * | | * | | * | | * | | * | | * | | * | | * | | * |
| ATG | AAA | ATC | CTT | ATC | TTG | GTT | GCA | GCT | GGG | CTG | CTG | TTT | CTG | CCA | GTC | | | | |
| TAC | TTT | TAG | GAA | TAG | AAC | CAA | EGT | CGA | CCC | GAC | GAC | AAA | GAC | GGT | CAG | | | | |
| M | K | I | L | I | L | V | A | A | G | L | L | F | L | P | V> | | | | |
| 100 | | | 110 | | | | 120 | | | | 130 | | | | 140 | | | | |
| * | | * | * | | * | | * | | * | | * | | * | | * | | * | | * |
| ACT | GTT | TGC | CAA | AGT | GGC | ATA | AAT | GTT | TCA | GAC | AAC | TCA | GCA | AAG | CCA | | | | |
| TGA | CAA | ACG | GTT | TCA | CCG | TAT | TTA | CAA | AGT | CTG | TTG | AGT | CGT | TTC | GGT | | | | |
| T | V | C | Q | S | G | I | N | V | S | D | N | S | A | K | P> | | | | |
| 150 | | | 160 | | | | 170 | | | | 180 | | | | 190 | | | | |
| * | | * | * | | * | | * | | * | | * | | * | | * | | * | | * |
| ACC | TTA | ACT | ATT | AAG | AGT | TTT | AAT | GGG | GGT | CCC | CAA | AAT | ACC | TTT | GAA | | | | |
| TGG | AAT | TGA | TAA | TTC | TCA | AAA | TTA | CCC | CCA | GGG | GTT | TTA | TGG | AAA | CTT | | | | |
| T | L | T | I | K | S | F | N | G | G | P | Q | N | T | F | E> | | | | |
| 200 | | | 210 | | | | 220 | | | | 230 | | | | 240 | | | | |
| * | | * | * | | * | | * | | * | | * | | * | | * | | * | | * |
| GAA | TTC | CCA | CTT | TCT | GAC | ATA | GAG | GGC | TGG | ACA | GGA | GCC | ACC | ACA | ACT | | | | |
| CTT | AAG | GGT | GAA | AGA | CTG | TAT | CTC | CCG | ACC | TGT | CCT | CGG | TGG | TGT | TGA | | | | |
| E | F | P | L | S | D | I | E | G | W | T | G | A | T | T | T> | | | | |
| 250 | | | 260 | | | | 270 | | | | 280 | | | | 290 | | | | |
| * | | * | * | | * | | * | | * | | * | | * | | * | | * | | * |
| ATA | AAA | GCG | GAG | TGT | CCC | GAG | GAC | AGT | ATT | TCA | ACT | CTC | CAC | GTG | AAT | | | | |
| TAT | TTT | CGC | CTC | ACA | GGG | CTC | CTG | TCA | TAA | AGT | TGA | GAG | GTG | CAC | TTA | | | | |
| I | K | A | E | C | P | E | D | S | I | S | T | L | H | V | N> | | | | |
| 300 | | | 310 | | | | 320 | | | | 330 | | | | | | | | |
| * | | * | * | | * | | * | | * | | * | | * | | * | | * | | * |
| AAT | GCT | ACC | ATA | GGA | TAC | CTG | AGA | AGT | TCC | TTA | AGT | ACC | CAA | GTG | ATA | | | | |
| TTA | CGA | TGG | TAT | CCT | ATG | GAC | TCT | TCA | AGG | AAT | TCA | TGG | GTT | CAC | TAT | | | | |
| N | A | T | I | G | Y | L | R | S | S | L | S | T | Q | V | I> | | | | |
| 340 | | | 350 | | | | 360 | | | | 370 | | | | 380 | | | | |
| * | | * | * | | * | | * | | * | | * | | * | | * | | * | | * |
| CCT | GCC | ATC | TAT | ATC | CTG | CTG | TTT | GTG | GTT | GGT | GTA | CCA | TCC | AAC | ATC | | | | |
| GGA | CGG | TAG | ATA | TAG | GAC | GAC | | | | | | | | | | | | | |

FIG. 2-2

| | | | | |
|------------|-------------|------------|------------|------------|
| 660 | 670 | 680 | 690 | 700 |
| * * | * * | * * | * * | * * |
| CGACGCGTGC | GANTCCCCAT | CATCCTTCCG | ATTCTACTAC | TTCGTCTCCT |
| 710 | 720 | 730 | 740 | 750 |
| * * | * * | * * | * * | * * |
| TAGCATTCTT | TGGGTTCCCTC | ATCCCGTTTG | TGATCATCAT | CTTCTGTAC |
| 760 | 770 | 780 | 790 | 800 |
| * * | * * | * * | * * | * * |
| ACGACTCTCA | TCCACAAACT | TAAATCAAAA | GATCNGATAT | GGCTGGGCTA |
| 810 | 820 | 830 | 840 | 850 |
| * * | * * | * * | * * | * * |
| CATCAAGGCC | GTCCTCCTCA | TCCTTGTA | TTTCACCATC | TGCTTCCCCC |
| 860 | 870 | 880 | 890 | 900 |
| * * | * * | * * | * * | * * |
| CCACCAAG-- | ----GATATC | TGGGAAGACG | TACATGCTTG | GCTGACTTGT |
| 910 | 920 | 930 | 940 | 950 |
| * * | * * | * * | * * | * * |
| GCATGGCACC | ATCAGCTCAA | TTTTTAATTT | TTTAATTTTA | ATTTAATTTA |
| 960 | 970 | 980 | 990 | 1000 |
| * * | * * | * * | * * | * * |
| ATTTTATGTT | TTTGAGACAG | AGCCTCACTG | TGTAGTCCTG | GCTGGCCTGG |
| 1010 | 1020 | 1030 | 1040 | 1050 |
| * * | * * | * * | * * | * * |
| CTGGTTCTCT | ATTTAGACCA | GGTTAGCCTT | GAACTCACAG | AGATCTGCCT |
| 1060 | 1070 | 1080 | 1090 | 1100 |
| * * | * * | * * | * * | * * |
| GCTTCTGCCT | CCCAAGTGCT | GGGTTCAACC | AGGTCTGGCA | AGCGCTCCAT |
| 1110 | 1120 | | | |
| * * | * * | | | |
| TTTTCAGCTC | CTCTGCAACA | GTGC | | |

600 610 620 630 640 650 660 670 680 690 700 710 720 730 740 750 760 770 780 790 800 810 820 830 840 850 860 870 880 890 900 910 920 930 940 950 960 970 980 990 1000 1010 1020 1030 1040 1050 1060 1070 1080 1090 1100 1110 1120

FIG. 3-1

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----|---|
| | | | | | | | | | | | | | | | | |
| | * | | | | | | | | | | | | | | | |
| TGC | TCC | ATG | ATT | TTA | CAG | ATT | TCA | TAA | CGT | TTA | AGA | GAC | GGG | ACT | CAG | |
| ACG | AGG | TAC | TAA | AAT | GTC | TAA | AGT | ATT | GCA | AAT | TCT | CTG | CCC | TGA | GTC | |
| C | S | M | I | L | Q | I | S | * | R | L | R | D | G | T | Q> | |
| 50 | | | 60 | | | 70 | | | | 80 | | | 90 | | | |
| * | | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| GTC | ATC | AAA | ATG | AAA | GCC | CTC | ATC | TTT | GCA | GCT | GCT | GGC | CTC | CTG | CTT | |
| CAG | TAG | TTT | TAC | TTT | CGG | GAG | TAG | AAA | CGT | CGA | CGA | CCG | GAG | GAC | GAA | |
| V | I | K | M | K | A | L | I | F | A | A | A | G | L | L | L> | |
| 100 | | | 110 | | | 120 | | | | 130 | | | 140 | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| CTG | TTG | CCC | ACT | TTT | TGT | CAG | AGT | GGC | ATG | GAA | AAT | GAT | ACA | AAC | AAC | |
| GAC | AAC | GGG | TGA | AAA | ACA | GTC | TCA | CCG | TAC | CTT | TTA | CTA | TGT | TTG | TTG | |
| L | L | P | T | F | C | Q | S | G | M | E | N | D | T | N | N> | |
| 150 | | | 160 | | | 170 | | | | 180 | | | 190 | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| TTG | GCA | AAG | CCA | ACC | TTA | CCC | ATT | AAG | ACC | TTT | CGT | GGA | GCT | CCC | CCA | |
| AAC | CGT | TTC | GGT | TGG | AAT | GGG | TAA | TTC | TGG | AAA | GCA | CCT | CGA | GGG | GGT | |
| L | A | K | P | T | L | P | I | K | T | F | R | G | A | P | P> | |
| 200 | | | 210 | | | 220 | | | | 230 | | | 240 | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| AAT | TCT | TTT | GAA | GAG | TTC | CCC | TTT | TCT | GCC | TTG | GAA | GGC | TGG | ACA | GGA | |
| TTA | AGA | AAA | CTT | CTC | AAG | GGG | AAA | AGA | CGG | AAC | CTT | CCG | ACC | TGT | CCT | |
| N | S | F | E | E | F | P | F | S | A | L | E | G | W | T | G> | |
| 250 | | | 260 | | | 270 | | | | 280 | | | | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| GCC | ACG | ATT | ACT | GTA | AAA | ATT | AAG | TGC | CCT | GAA | GAA | AGT | GCT | TCA | CAT | |
| CGG | TGC | TAA | TGA | CAT | TTT | TAA | TTC | ACG | GGA | CTT | CTT | TCA | CGA | AGT | GTA | |
| A | T | I | T | V | K | I | K | C | P | E | E | S | A | S | H> | |
| 290 | | | 300 | | | 310 | | | | 320 | | | 330 | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| CTC | CAT | GTG | AAA | AAT | GCT | ACC | ATG | GGG | TAC | CTG | ACC | AGC | TCC | TTA | AGT | |
| GAG | GTA | CAC | TTT | TTA | CGA | TGG | TAC | CCC | ATG | GAC | TGG | TCG | AGG | AAT | TCA | |
| L | H | V | K | N | A | T | M | G | Y | L | T | S | S | L | S> | |
| 340 | | | 350 | | | 360 | | | | 370 | | | 380 | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| ACT | AAA | CTG | ATA | CCT | GCC | ATC | TAC | CTC | CTG | GTG | TTT | GTA | GTT | GGT | GTC | |
| TGA | TTT | GAC | TAT | GGA | CGG | TAG | ATG | GAG | GAC | CAC | AAA | CAT | CAA | CCA | CAG | |
| T | K | L | I | P | A | I | Y | L | L | V | F | V | V | G | V> | |
| 390 | | | 400 | | | 410 | | | | 420 | | | 430 | | | |
| * | * | * | * | | * | * | * | | * | * | * | * | * | * | * | * |
| CCG | GCC | AAT | GCT | GTG | ACC | CTG | TGG | ATG | CTT | TTC | TTC | AGG | ACC | AGA | TCC | |
| GGC | CGG | TTA | CGA | CAC | TGG | GAC | ACC | TAC | GAA</ | | | | | | | |

FIG. 3-2

| 440 | | | | 450 | | | | 460 | | | | 470 | | | | 480 | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|--|--|
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | |
| ATC | TGT | ACC | ACT | GTA | TTC | TAC | ACC | AAC | CTG | GCC | ATT | GCA | GAT | TTT | CTT | | | | |
| TAG | ACA | TGG | TGA | CAT | AAG | ATG | TGG | TTG | GAC | CGG | TAA | CGT | CTA | AAA | GAA | | | | |
| I | C | T | T | V | F | Y | T | N | L | A | I | A | D | F | L> | | | | |
| 490 | | | | 500 | | | | 510 | | | | 520 | | | | | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | | | |
| TTT | TGT | GTT | ACA | TTG | CCC | TTT | AAG | ATA | GCT | TAT | CAT | CTC | AAT | GGG | AAC | | | | |
| AAA | ACA | CAA | TGT | AAC | GGG | AAA | TTC | TAT | CGA | ATA | GTA | GAG | TTA | CCC | TTG | | | | |
| F | C | V | T | L | P | F | K | I | A | Y | H | L | N | G | N> | | | | |
| 530 | | | | 540 | | | | 550 | | | | 560 | | | | 570 | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | |
| AAC | TGG | GTA | TTT | GGA | GAG | GTC | CTG | TGC | CGG | GCC | ACC | ACA | GTC | ATC | TTT | | | | |
| TTG | ACC | CAT | AAA | CCT | CTC | CAG | GAC | ACG | GCC | CGG | TGG | TGT | CAG | TAG | AAG | | | | |
| N | W | V | F | G | E | V | L | C | R | A | T | T | V | I | F> | | | | |
| 580 | | | | 590 | | | | 600 | | | | 610 | | | | 620 | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | | | |
| TAT | GGC | AAC | ATG | TAC | TGC | TCC | ATT | CTG | CTC | CTT | GCC | TGC | ATC | AGC | ATC | | | | |
| ATA | CCG | TTG | TAC | ATG | ACG | AGG | TAA | GAC | GAG | GAA | CGG | ACG | TAG | TCG | TAG | | | | |
| Y | G | N | M | Y | C | S | I | L | L | L | A | C | I | S | I> | | | | |
| 630 | | | | 640 | | | | 650 | | | | 660 | | | | 670 | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | |
| AAC | CGC | TAC | CTG | GCC | ATC | GTC | CAT | CCT | TTC | ACC | TAC | CGG | GGC | CTG | CCC | | | | |
| TTG | GCG | ATG | GAC | CGG | TAG | CAG | GTA | GGA | AAG | TGG | ATG | GCC | CCG | GAC | GGG | | | | |
| N | R | Y | L | A | I | V | H | P | F | T | Y | R | G | L | P> | | | | |
| 680 | | | | 690 | | | | 700 | | | | 710 | | | | 720 | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | | | |
| AAG | CAC | ACC | TAT | GCC | TTG | GTA | ACA | TGT | GGA | CTG | GTG | TGG | GCA | ACA | GTT | | | | |
| TTC | GTG | TGG | ATA | CGG | AAC | CAT | TGT | ACA | CCT | GAC | CAC | ACC | CGT | TGT | CAA | | | | |
| K | H | T | Y | A | L | V | T | C | G | L | V | W | A | T | V> | | | | |
| 730 | | | | 740 | | | | 750 | | | | 760 | | | | | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | | | |
| TTC | TTA | TAT | ATG | CTG | CCA | TTT | TTC | ATA | CTG | AAG | CAG | GAA | TAT | TAT | CTT | | | | |
| AAG | AAT | ATA | TAC | GAC | GGT | AAA | AAG | TAT | GAC | TTC | GTC | CTT | ATA | ATA | GAA | | | | |
| F | L | Y | M | L | P | F | F | I | L | K | Q | E | Y | Y | L> | | | | |
| 770 | | | | 780 | | | | 790 | | | | 800 | | | | 810 | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | | | |
| GTT | CAG | CCA | GAC | ATC | ACC | ACC | TGC | CAT | GAT | GTT | CAC | AAC | ACT | TGC | GAG | | | | |
| CAA | GTC | GGT | CTG | TAG | TGG | TGG | ACG | GTA | CTA | CAA | GTG | TTG | TGA | ACG | CTC | | | | |
| V | Q | P | D | I | T | T | C | H | D | V | H | N | T | C | E> | | | | |
| 820 | | | | 830 | | | | 840 | | | | 850 | | | | 860 | | | |
| * | * | * | * | * | * | * | * | * | * | * | * | * | * | * | | | | | |

FIG. 4-1

| | | | | |
|------------|------------|-------------|------------|------------|
| 10 | 20 | 30 | 40 | 50 |
| * * | * * | * * | * * | * * |
| -ACAGGCATG | GAAAATGATA | CAAACAACCTT | GGCAAAGCCA | ACCTTACCCA |
| 60 | 70 | 80 | 90 | 100 |
| * * | * * | * * | * * | * * |
| TTAAGACCTT | TCGTGGAGCT | CCCCCAAATT | CTTTTGAAGA | GTTCCCTTTT |
| 110 | 120 | 130 | 140 | 150 |
| * * | * * | * * | * * | * * |
| TCTGCCTTGG | AAGGCTGGAC | AGGAGCCACG | ATTACTGTAA | AAATTAAGTG |
| 160 | 170 | 180 | 190 | 200 |
| * * | * * | * * | * * | * * |
| CCCTGAAGAA | AGTGCTTCAC | ATCTCCATGT | GAAAAATGCT | ACCATGGGGT |
| 210 | 220 | 230 | 240 | 250 |
| * * | * * | * * | * * | * * |
| ACCTGACCAG | CTCCTTAAGT | ACTAAACTGA | TACCTGCCAT | CTACCTCCTG |
| 260 | 270 | 280 | 290 | 300 |
| * * | * * | * * | * * | * * |
| GTGTTTGTAG | TTGGTGTCCC | GGCCAATGCT | GTGACCCTGT | GGATGCTTTT |
| 310 | 320 | 330 | 340 | 350 |
| * * | * * | * * | * * | * * |
| CTTCAGGACC | AGATCCATCT | GTACCACTGT | ATTCTACACC | AACCTGGCCA |
| 360 | 370 | 380 | 390 | 400 |
| * * | * * | * * | * * | * * |
| TTGCAGATTT | TCTTTTTTGT | GTTACATTGC | CCTTTAAGAT | AGCTTATCAT |
| 410 | 420 | 430 | 440 | 450 |
| * * | * * | * * | * * | * * |
| CTCAATGGGA | ACAACTGGGT | ATTTGGAGAG | GTCCTGTGCC | GGGCCACCAC |
| 460 | 470 | 480 | 490 | 500 |
| * * | * * | * * | * * | * * |
| AGTCATCTTC | TATGGCAACA | TGTACTGCTC | CATTCTGCTC | CTTGCCTGCA |
| 510 | 520 | 530 | 540 | 550 |
| * * | * * | * * | * * | * * |
| TCAGCATCAA | CCGCTACCTG | GCCATCGTCC | ATCCTTTCAC | CTACCGGGGC |
| 560 | 570 | 580 | 590 | 600 |
| * * | * * | * * | * * | * * |
| CTGCCCAAGC | ACACCTATGC | CTTGGTAACA | TGTGGACTGG | TGTGGGCAAC |
| 610 | 620 | 630 | 640 | 650 |
| * * | * * | * * | * * | * * |
| AGTTTTCTTA | TATATGCTGC | CATTTTTTCAT | ACTGAAGCAG | GAATATTATC |

FIG. 5A

hPAR3-1 MKA LIFAAAGLLLLP TFCQSGMENDINNLA KP TLPK / TFRGAPPN SFEFFPSALEGTGATITVKIKC PEESASHLHVKNATMG
hPAR1-1 MGPRR LLLVAACFSLCGP LLSARTRARRPESKATNATLDP / SFLLRNPNDKYEPFWEDEEKESGLTEYRLVSINKSSPLQQLPAFISEDASG
hPAR2-1 MRSPSAWLLGAAILLA ASLSCSGTIQG TNRSSKGR / SLIGKYDGTSHVTGKGVTV ETVFSVDEFSAS

hPAR3-87 YLTSSLSTKLIPAIYLLVFVGVGPANAVTLWMLFFRTR SICTTVFYTNLAIAADFLFCVTLPFKIAHYHLNGNNWVGEVLCRATTVIFYGNMYCSILLACISINRYLAI
hPAR1-95 YLTSSWLTLFVPSVYTGTVFVSLPLNIMAIVVILKMKVKKPAVVYMLHLATADVLFSVLPFKISYYFSGDWQFGSELCRFVTAAFYCNMYASILLMTVISIDRFLAV
hPAR2-68 VLTGKLTTVFLPIVYTIIVFVGLPSNGMALWVFLFRTKKKHPAVIYMANLALADLLSVIWFPLKIAHYIHGNNWIYGEALCNVLIGFFYGNMYCSILFMTCLSVQRYWVI

hPAR3-196 VHPFTYRGLPKHTYALVTCGLVWATVFLYMLPFFILKQEYLVQPDITTHCHDVHNTCESSPPFQLYYFISLAFFGLIPFVLIICYAAIIRTLNA YDHRWLWYV
hPAR1-205 VYPMQSLSWRTLGRASFTCLAIWALAIAGVPLVLKEQTIQVPLNITTHCHDVNLTLLEG YVAYYFSAFSAVFFVPLIITVICYCIIIRCLSSSAVANRSKK SRAL
hPAR2-178 VNPMGHSRKKANIAIGI SLAIWLLILLVTIPLYVVKQTI FIPALNITTHCHDVLPQLLVGD MFNYFLSLAIGVFLFPALFTASAYVLMIRMLRSSAMDENSEKKRKRAI

hPAR3-301 KASLLILVIFTICFAPSNIILIIHHANYYYNNI DGLYFIYIALCLGSLNSCLDPFLYFLMSKTRNHSTAYLTK
hPAR1-313 FLAAVFCIFIIICFGPTNVLLIAHYSFLSHTSTTEAAYFAYLLCVCVSSISSCIDPLIYYASSECQRYVYSILCKEKSSDPSSYNSSGQLMASKMDTCSSNLNNSIYKFLLT
hPAR2-287 KLIVTVLAMYLCFTPSNLLLVVHY FLIKSQGQSHVYALYIVALCLSTLNSCIDPFFVYFVSHDFRDHAKNALLCRSVRTVKMQVSLTSKKHSRKSSSYSSSSTTVKTSY

FIG. 5B

Hirudin C-tail ..DFEEIPEEYLQ
hPAR3- 34-62 ..TLPK / TFRGAPPN SFEFFPSALEGTGA..
hPAR1- 37-65 ..TLDPR / SFLLRNPNDKYEPFWEDEEKESG..
hPAR2- 32-62 ..SSKGR / SLIGKYDGTSHVTGKGVTVFVSVD..

*SURFACE STAINING OF M1-epitope
+/- α -thrombin AT 37°C FOR 5 MINUTES*

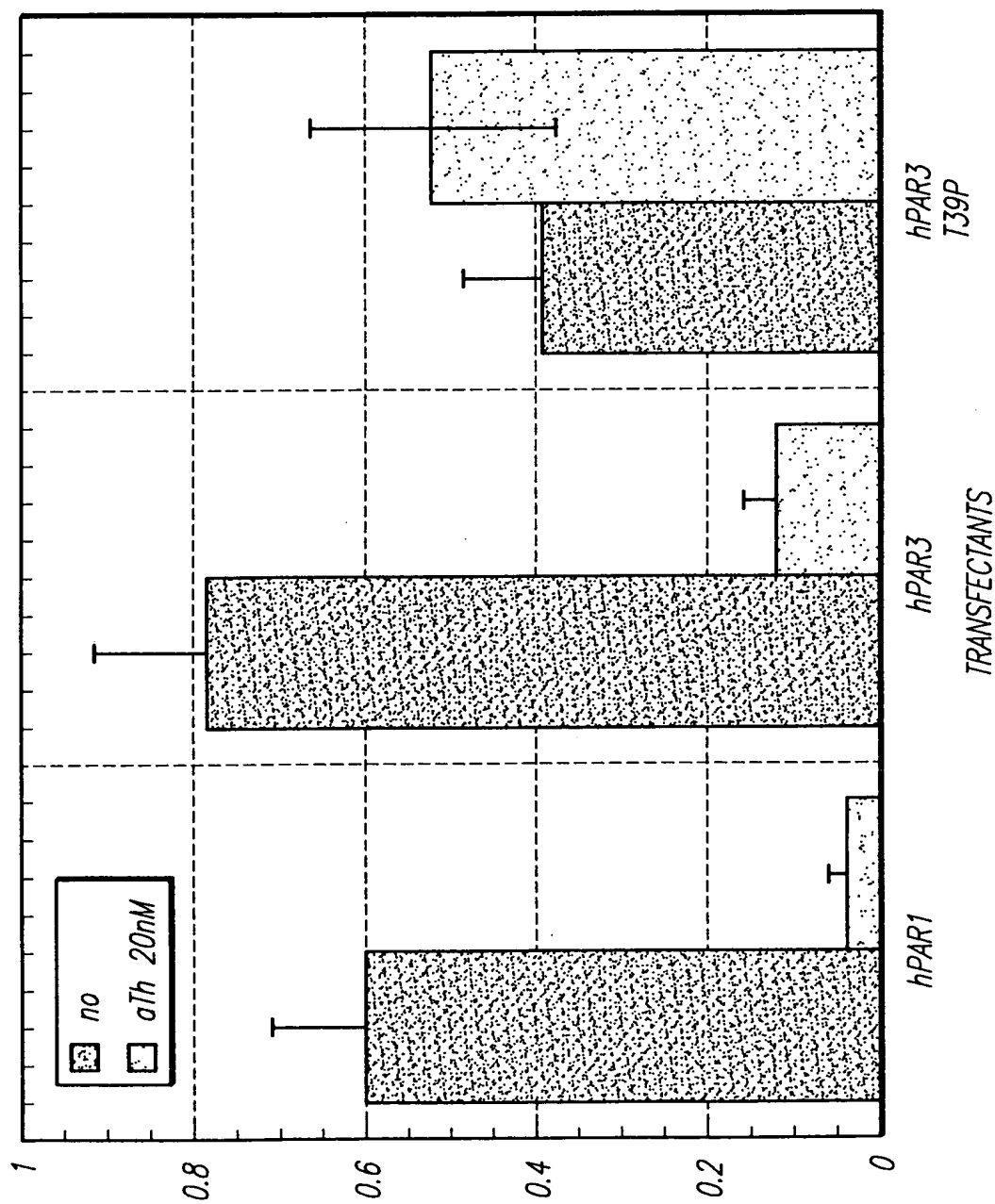


FIG. 6

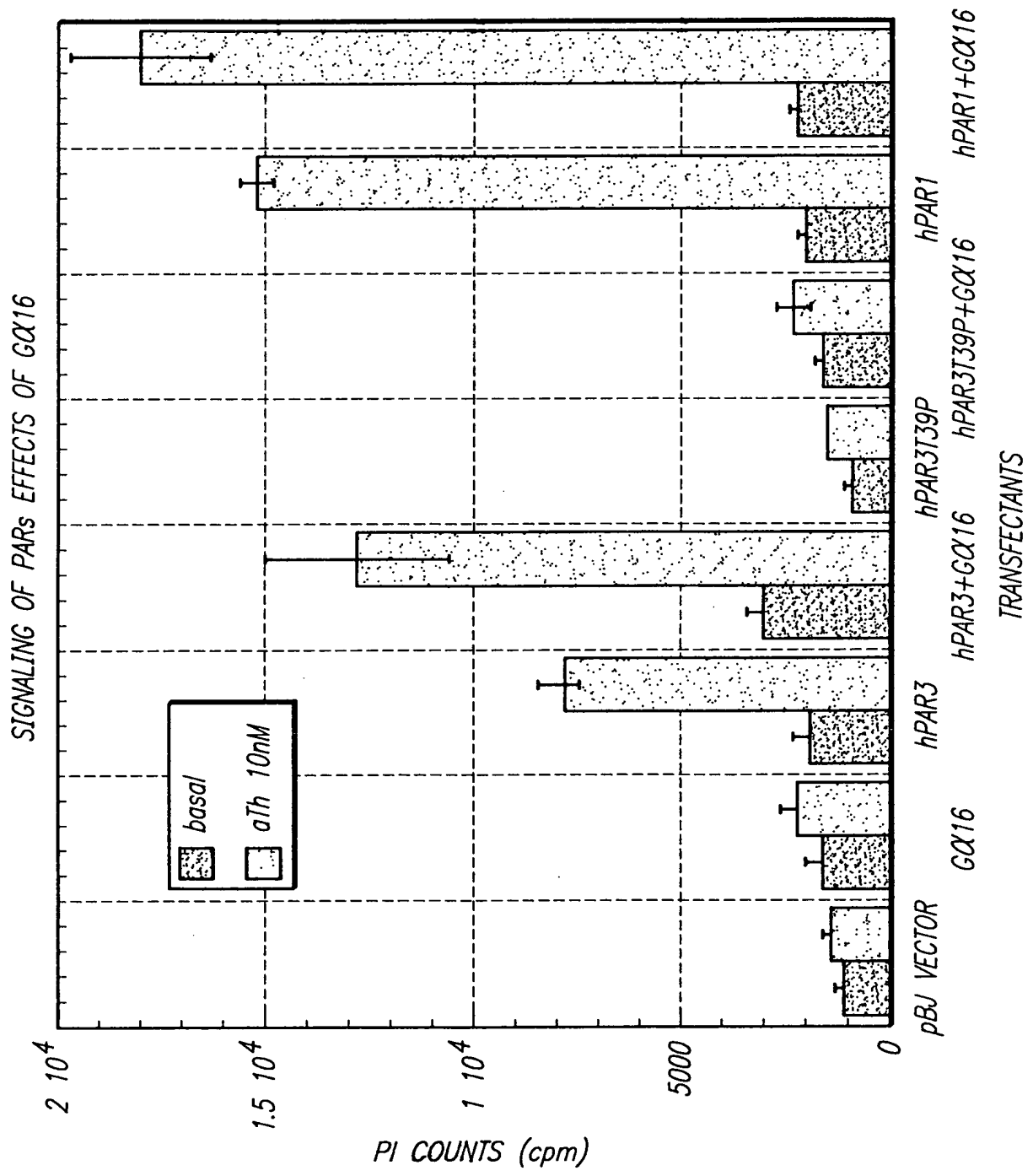


FIG. 7

FIG. 8

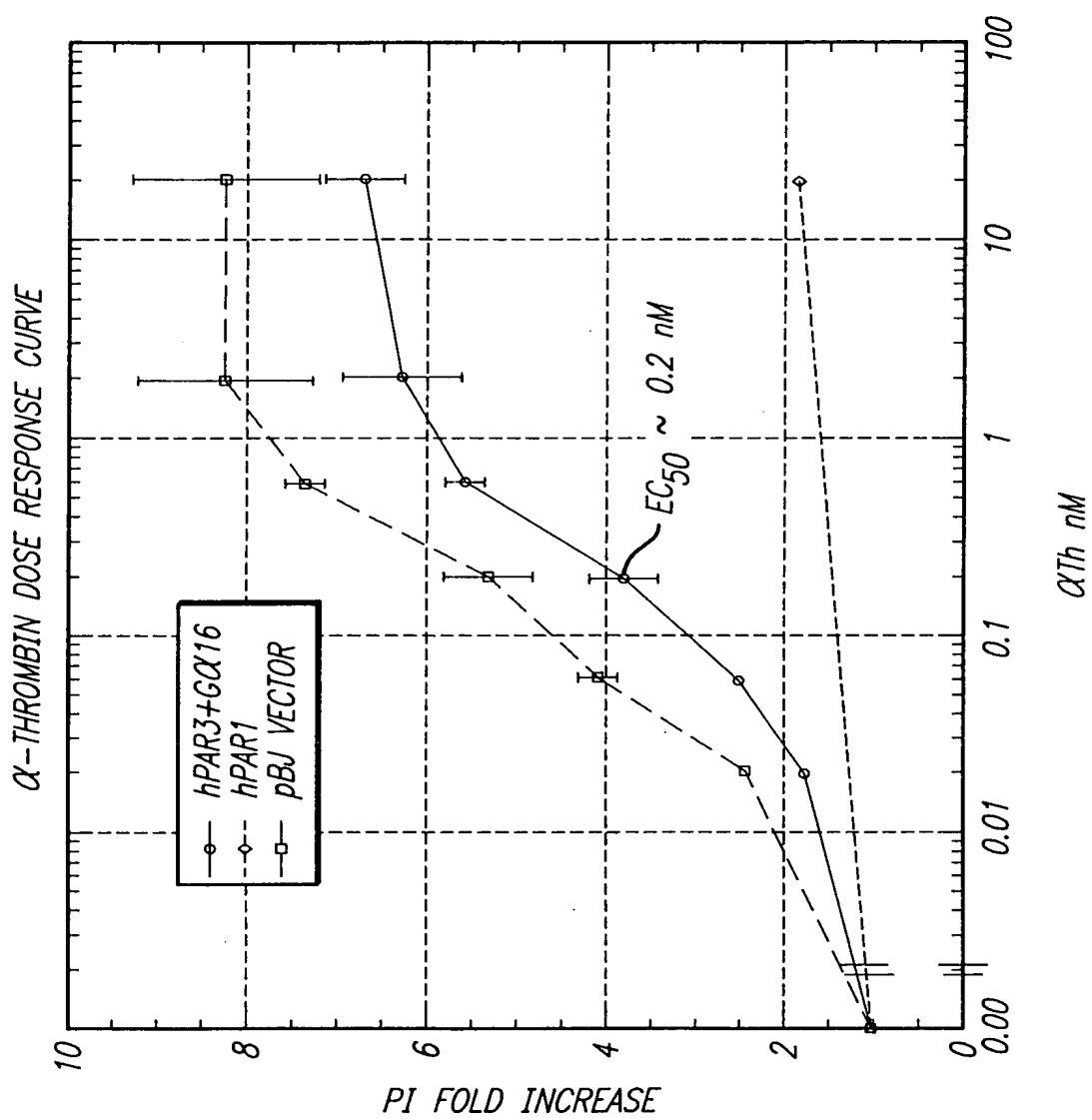
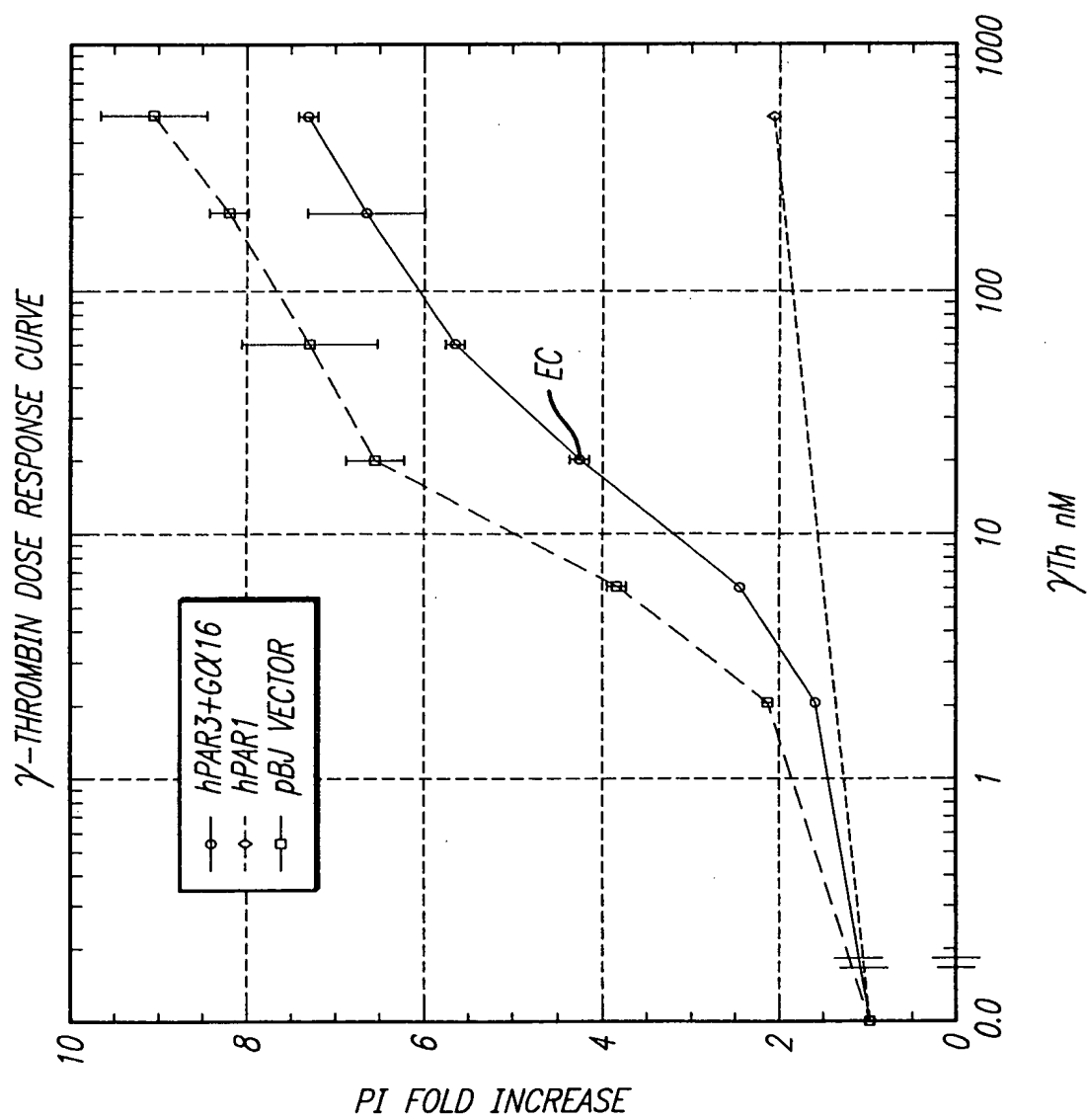


FIG. 9



6007-6926

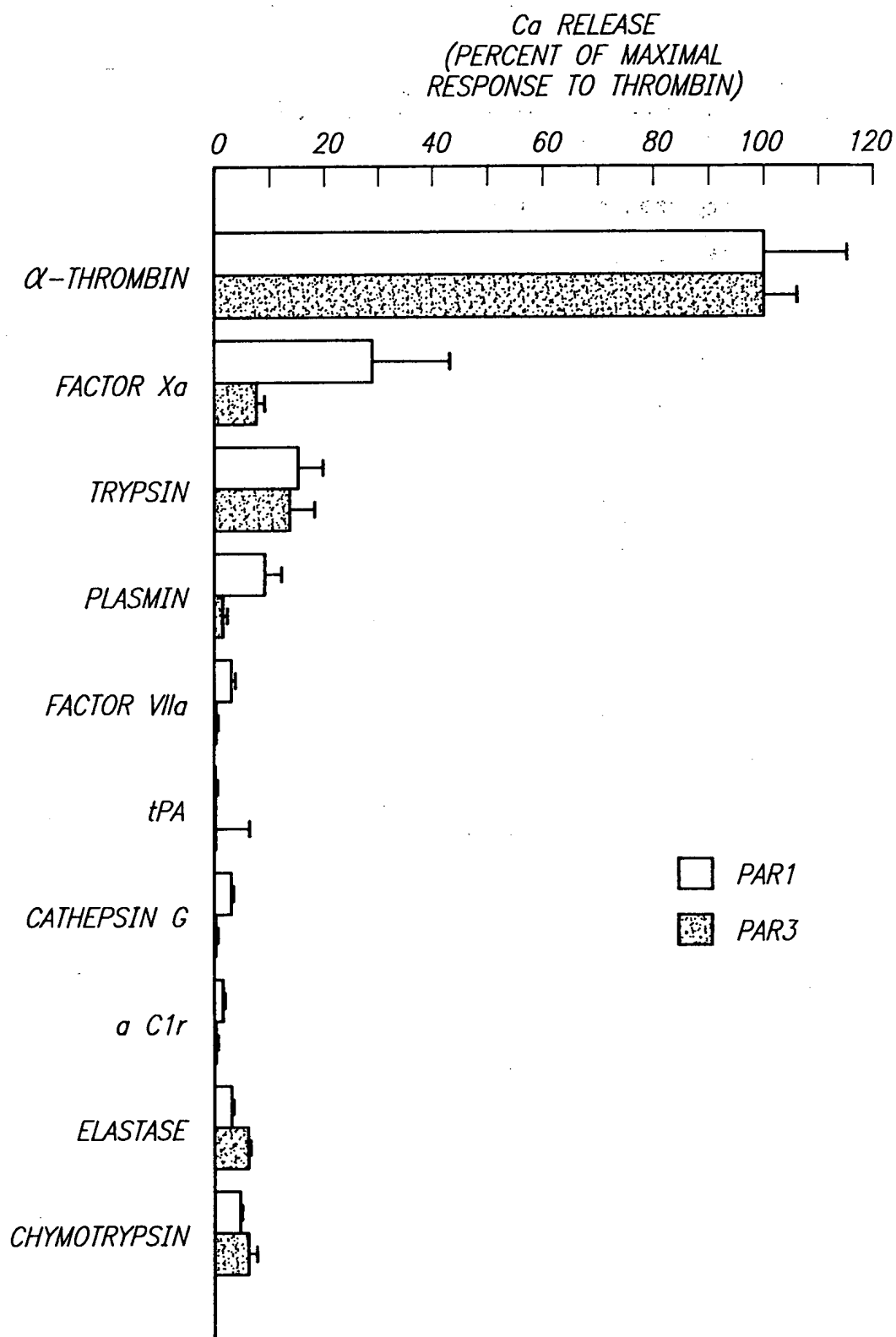


FIG. 10